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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WILLIAMS, LEONARD M	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 01/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/995,911	MAZESS, RICHARD B.	
	Examiner	Art Unit	
	Leonard M. Williams	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *56,57,59,60 and 63-73* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *56,57,59,60 and 63-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/22/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Status of Claims

The amendment received 10/05/2005 canceling claims 58 and 61-62 and amending claims 56 and 57 has been entered.

Claims 56-57, 59-60 and 63-73 are currently pending.

The terminal disclaimer filed on 10/05/2005 to overcome the obviousness-type double patenting rejection over claims 56-60 and 63-71 is sufficient to overcome the rejection and the ODP rejection is thus withdrawn.

Response to Arguments

Applicant's arguments with respect to claims 56-57, 59-60 and 63-73 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 60 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 60 depends from claim 56 wherein the active vitamin D compounds must be in accordance with formula III as set forth in claim 56. The examiner respectfully points out that claim 60 includes 24-hydroxyvitamin D_2 and 24-hydroxyvitamin D_4 as potential active vitamin D compounds and that these compounds are not encompassed by formula III. Correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 56-57, 59 and 63-71 are rejected under 35 U.S.C. 102(b) as being anticipated by Bishop et al. (WO94/05630) as evidenced by Goodman and Gilman's The Pharmaceutical Basis of Therapeutics, 7th edition..

Bishop et al. teach, on page 8 lines 33-37, 1α,24(S)-dihydroxy vitamin D_2 can be used in the treatment of hyperproliferative skin disorders and in the treatment of breast and colon cancer. On page 9 lines 1-17, Bishop et al. teach that 1α,24(S)-dihydroxy vitamin D_2 can be used in a variety of pharmaceutical compositions and formulations and that it is suitable for enteral, oral, parenteral or topical application; and that it has reduced side effects and lower toxicity as compared with known analogs of vitamin D_3.

Bishop et al. teach on page 10, that the compositions can be used in conjunction with epithelialization-inducing agents such as retinoids.

On page 11 lines 16-24, Bishop et al. teach that for oral administration the compound should be given in preferred amounts of 0.04-0.3 μg/kg/day (which corresponds to 19.6-147 μg/kg/week for a 70 kg person).

In examples 26-28, Bishop et al. demonstrate that 1α,24(S)-dihydroxy vitamin D_2 has activity in epidermal cell differentiation and proliferation of human keratinocytes

(example 26), the promotion of differentiation of HL-60 promyelocytes to monocytes (example 27), and potent antiproliferative activity against breast and colon cancer cell lines (example 28) anticipating the "...method of inhibiting hyperproliferation of malignant or neoplastic cells..." via administration of a vitamin D compounds of formula III of claim 56, the "...method...wherein the malignant cells are associated with cancers of the breast, colon..." of claim 57, the "...method...wherein the active vitamin D is 1α-hydroxyvitamin D_2 or 1α,24-dihydroxyvitamin D_2" of claim 59, the "...method...wherein the amount of the active vitamin D is administered..." of claim 63, the "...method...wherein the...vitamin D compound is administered parenterally or orally..." of claim 64, the "..method...wherein the amount of vitamin D compound is administered parenterally" of claim 65, the "...method...wherein the amount of vitamin D compound is administered intravenously" of claim 66, the "...method inhibiting hyperproliferation of malignant or neoplastic cell, comprising...co-administering...an active vitamin D compound and an...antineoplastic agent a bone agent, an antihypercalcemic agent or combinations..." of claim 67, the"...method...are episodically co-administered..."of claim 68, the "...method...wherein the agent is an antineoplastic agent" of claim 69, the "...method...wherein the antineoplastic agent...and the active vitamin D is given concurrently..." of claim 70, and the "...method...wherein the antineoplastic agent is...or any other antineoplastic agent or combinations thereof" of claim 71.

Goodman and Gilman's The Pharmaceutical Basis of Therapeutics, 7th edition teaches on pages 1573-1580, that the retinoids (including retinol, retinal, and retinoic acid) have activity as anticancer agents. On page 1580 it is disclosed that following the

binding of retinoic acid to the CRABP complex in the cytosol the complex migrates inducing a cascade of specific biochemical events. Correlation has been found between the CRABP and the antitumor effects of the retinoids.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 72-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bishop et al. as applied to claim 56-57, 59 and 63-71 above, and further in view of Schwender et al. (US Patent 5300687).

Bishop et al. is as set forth above.

Bishop et al. does not teach a method wherein the bone agent is a bisphosphonate, nor a method wherein a vitamin D compound, an antineoplastic agent, and an antihypercalcemic agent are co-administered.

Schwender et al. teaches, in col. 1 lines 22-30, that osteoporosis treatments include estrogen replacement, bisphosphonates, vitamin D metabolites and calcium supplements.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use bisphosphonates in conjunction with the vitamin D and retinoic acid compounds of Bishop et al. as the bisphosphonates are known compounds useful in the treatment of bone disorders.

The examiner respectfully points out the following from MPEP 2144.06: "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re* Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Claim 60 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bishop et al. as applied to claims 56-57, 59 and 63-71 above, and further in view of Ostrem et al. (Induction of Monocytic Differentiation of HL-60 Cells by 1,25-Dihydroxyvitamin D Analogs, The Journal of Biological Chemistry, 1987, Vol. 262, No. 29, pp. 14164-14171).

Bishop et al. is as set forth above.

Bishop et al. does not teach 1α,25-dihydroxyvitamin D_2.

Ostrem et al. teach, on page 14164 column 2, that previous studies have indicated that the ability of vitamin D metabolites to induce HL-60 cell differentiation correlates with the binding affinity of the metabolite for the 1,25-$(OH)_2D_3$ receptor. On page 14169, Ostrem et al. teach that the stereochemistry of the hydroxyl group at the C-1 position is important as epimerization of 1-α to 1-β abolishes activity. Additionally on page 14169 column 2, Ostrem et al. teach that vitamin D_2 compounds (1l, 1i and 2b in Figure 1 and Table I) are synthetic analogs of vitamin D_3 and that vitamin D_2 and D_3 are metabolized in similar manners and that 1α,25-dihydroxyvitamin D_2 (1i) is as biologically active and has equivalent affinity for the intestinal receptor as 1α,25-dihydroxyvitamin D_3 in mammals. Table I demonstrates the activities of the vitamin D_2 compounds in a variety of HL-60 differentiation studies and their realative activity to 1,25-dihydroxyvitamin D_3. On page 14170, Ostrem et al. indicate that the vitamin D_2 side chain is a better structure in inducing HL-60 differentiation than D_3.

It would have been obvious to one of ordinary skill in the art at the time the invention was made that 1α,25-dihydroxyvitamin D_2 and its related compounds could be used in Bishop et al.'s compositions and methods for the treatment of bone disorders and in the treatment of cancer. One would have been motivated to use Ostrem et al.'s D_2 compounds in Bishop et al.'s methods and compositions as the D_2 compounds showed better induction of differentiation in HL-60 cell lines and thus would have better efficacy in the treatment of bone disorders and cancer. Additionally Bishop et al. on page 3 first paragraph, indicate that vitamin D_2 compounds show less toxicity than equivalent vitamin D_3 compounds.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leonard M. Williams whose telephone number is 571-272-0685. The examiner can normally be reached on MF 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

LMW

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER